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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,375	09/24/2001	Ikunoshin Kato	KATO18	8012

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EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 12/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,375	KATO ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,42 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,42 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 9/29/2005. The amendment filed 9/29/2005 is acknowledged and has been entered. Claims 8, 42 and 43 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claims 8, 42 and 43 are examined herein.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 8, 42 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asada et al. (EP 0 870 839 A1) in view of Asada et al. (Journal of Biochemistry, 1998; Vol. 123, pages 1041-1047) and further in view of Kubota et al. (Journal of Dermatological Science, 1996; Vol. 12, pages 36-43) and Qin et al. (Journal of Clinical Immunology, 1993; Vol. 13, No. 2, pages 152-161).

The instant claims are drawn to a composition for transfecting a cell at a site at a site of vascularization in vivo comprising (1) a retrovirus that contains a gene to be transfected, (2) CH-296, and (3) human umbilical vein endothelial (HUVEC) cells used as vehicles (new limitation of claim 8); wherein the gene to be transected encodes a therapeutic protein such as an enzyme or cytokine.

It is noted that the limitations, "an effective amount for transfecting a cell at a site of vascularization in vivo" do not appear to be explicitly defined in the specification. As such, given the broadest reasonable interpretation of the claims consistent with the specification, the limitation "an effective amount for transfecting a cell at a site of vascularization in vivo" is interpreted as encompassing any amount.

Claim 8 has been amended to indicate that the human umbilical vein endothelial cells (HUVEC) are vehicles. It is noted that the indication the HUVECs are vehicles, does not impart any structural change to the claimed composition. That is, the new limitation does not change the structure of the claimed composition, the limitation only indicates the HUVECs are "vehicles". As such, the instant claims are still obvious over Asada et al. (EP 0 870 839 A1), Asada et al. (Journal of Biochemistry, 1998), Kubota et al. (1996) and Qin et al. (1993) for the reasons of record, which are reiterated below.

Asada et al. (EP 0 870 839 A1) teaches a method for introducing a gene into a target cell using a composition comprising (1) a retrovirus, (2) a cell, and (3) a functional material having (i) a retrovirus binding domain, and (ii) a target cell binding domain (e.g., see abstract; page 5 lines 35-41). Asada et al. (EP 0 870 839 A1) specifically teaches that the functional material having affinity for the retrovirus and target cell can be CH-296 (e.g., see page 24, lines 40-55). Asada et al. (EP 0 870 839 A1) also teaches that the retrovirus can comprise a gene encoding an enzyme (e.g., see p. 6, lines 41-45), and that the target cell can be any one of a number of different cells, including angio-endothelial cells (e.g., see page 5, lines 46-53). Therefore, Asada et al. (EP 0 870 839 A1) teaches a composition comprising (1) a retrovirus, (2) CH-296, and (3) an angio-endothelial cell wherein the retrovirus encodes a therapeutic protein that is an enzyme.

It is noted that Asada et al. (EP 0 870 839 A1) teaches that the functional material having affinity for the target cell can be used to target a retrovirus to a cell that expresses the VLA-4 or VLA-5 antigen (e.g., see page 4, lines 21-24; page 8, lines 42-55; page 12, lines 43-47; page 6, lines 10-12; etc.).

Asada et al. (EP 0 870 839 A1) does not explicitly teach that CH-296 binds to VLA-4 or that the cells are human umbilical vein cord (HUVEC) cells.

However, Asada et al. (1998) teaches that CH-296 is a recombinant polypeptide comprising a CS1 site which is recognized by VLA-4. Asada et al. (1998) also specifically teaches that CH-296 can enhance gene transfer through binding to both retrovirus particles and target cells that express integrins VLA-5 and/or VLA-4 (e.g., see abstract; and page 1041, second column, last paragraph).

Kubota teaches that human umbilical vein endothelial cord (HUVEC) cells express the CDw49d antigen. It is noted that Kubota does not explicitly indicate that the CDw49d antigen is very late antigen-4 (VLA-4); however, Qin teaches that CDw49d is very late antigen-4 (VLA-4) (e.g., see abstract; page 153, first column end of first full paragraph; page 155, under "Expression of Adhesion Molecules"; etc.).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Asada et al. (EP 0 870 839 A1), Asada et al. (1998), Kubota and Qin to create a composition comprising a retrovirus that expresses an enzyme, CH-296, and an angio-endothelial cell (as taught by Asada) wherein the angio-endothelial cell is a human umbilical vein endothelial cord (HUVEC) cell (as taught by Kubota and Beekhuizen), with a reasonable expectation of success. It is noted that the HUVEC cells in

the composition made by combining the indicated references would, by necessity, be "vehicles" which comprise the retrovirus and CH-296.

One of ordinary skill in the art would have been motivated to make the claimed composition in view of the teachings that (1) the CH-296 can be used to enhance transfection of VLA-4 angio-endothelial cells with a retrovirus encoding an enzyme, and (2) HUVEC cells are angio-endothelial cells that express VLA-4/CDw49d antigen.

Response to Arguments

Applicant's arguments filed 99/29/2005 have been fully considered but they are not persuasive.

Applicants point out that support for the new limitation can be found in the specification as filed at page 19, lines 1-14.

Support for the new limitation is acknowledged.

Applicants point out that that claim 8 has been amended to recite that human umbilical vein endothelial cells are used as vehicles, and argue that none of the cited references discloses or suggests using human umbilical vein endothelial cells as vehicles for gene transfer.

In response, Applicant is reminded that MPEP 2112.01 indicates, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of

the applicant and the prior art are the same, the applicant has the burden of showing that they are not.'"

It is respectfully pointed out that the cited references teach all of the structural limitations of the claims. That is, the cited references teach a composition comprising (1) a retrovirus that contains a gene to be transfected, (2) wherein the gene to be transfected is an enzyme which upon expression in the target cell is sufficient for treatment, (3) CH-296 and (4) a HUVEC cell.

Furthermore, regarding the new limitation that the HUVEC cell is a "vehicle" it is respectfully pointed out that one of ordinary skill in the art would recognize that a transfected cell would necessarily be a "vehicle" for delivering the nucleic acid that it has been transfected with (or the product that the nucleic acid encodes). For instance, see Rancourt et al. (Clinical Cancer Research, 1998) which specifically teaches that a HUVEC cell transfected with a nucleic acid which encodes HSV-Thymidine Kinase (an enzyme) can be used as "vehicle" for delivering the enzyme to the target tissue. Specifically, Rancourt teaches transfecting the HUVEC cells with AdCMVHSV-TK and administering the transfected HUVEC cells to cancer cells (in vitro and in vivo) where the delivery of the cells resulted in a cytotoxic effect on the cancer cells (e.g., see abstract). Rancourt concludes, "These findings suggest that endothelial cells may be used as a vehicle for the delivery of cytotoxicity (bystander effect) in molecular chemotherapy" (See abstract). Thus one of ordinary skill in the art, with the knowledge of Rancourt would clearly recognize a HUVEC cell transfected with an nucleic acid encoding a therapeutic gene (such as an enzyme) would necessarily be a "vehicle" for delivering the therapeutic gene or gene product.

Applicants are reminded that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to

patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In the instant case the intended use of the composition (for transfecting a cell at a site of vascularization *in vivo*) does not impart any structural difference between the claimed invention and the prior art.

Furthermore, a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Therefore, Applicants arguments are not persuasive.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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